many applications, larger dimensions on the scale of millimeters may be used. Similarly, chambers (sometimes also referred to herein as "wells") in the substrates often will have larger dimensions, on the scale of a few millimeters.

[0057] The microchannels may have any shape, for example, it may be linear, serpentine, arc shaped and the like. The cross-section of the channel may be circular, semicircular, ellipsoid, square, rectangular, trapezoidal, or other convenient configurations.

[0058] In a preferred embodiment, the microfluidic devices of the invention comprise at least one magnetic microchannel. By "magnetic microchannel" herein is meant microchannels that are capable of capturing and retaining magnetic or magnetically labeled materials, or sorting magnetic materials according to their magnetic response. As described below in more detail, the magnetic microchannel is capable of capturing magnetic or magnetically labeled materials because of the existence of a local high gradient magnetic field within the microchannel.

[0059] Generally, the magnetic microchannels are bigger than the fluid microchannels described above, and the exact dimension of the magnetic microchannels depends on the design of the magnetic microchannel, the desired magnetic field gradients, the size of the magnetic beads that make up the magnetic microchannel, and the chamber volume for reactions. Large gradients can be designed into a large or small channel. If the gradients are highly local, the channel may be made shallower to bring the analytes closer to the surface. A channel with both local and more global gradients, described further below, may have greater depth. Thus, the depth of the magnetic microchannel range from about 10 μm to 1 mm, usually from 50 μm to 500 μm, and most preferably from 100 μm to 300 μm. The width of the channel range from about 100 μm to 10 mm, more preferably 2 mm to 5 mm.

[0060] The length of the magnetic microchannels also depends on the residence time of the component to be captured. Some of the factors that are to be taken into consideration are concentration of the component, volume of starting materials, flow speed, channel width, gradient strength, and magnetic labeling efficiency. The preferred length of the magnetic microchannel range from 100 μm to 100 cm, more preferably from 500 μm to 50 mm, and most preferably from 1 mm to 30 mm.

[0061] When magnetic or magnetically labeled materials pass through the magnetic microchannel, they experience a magnetic force that draws them towards locations of high magnetic field strength. At the same time, these material also experience a shear force that tends to pull the material away. The materials will generally be captured when the magnetic force is greater than the shear force, with surface interactions between the channel and sample also sometimes influencing capture. The magnetic force that pulls the magnetic or magnetically labeled material depends on the magnetization of the material, as well as the local magnetic field gradient or the magnetic force density the material is exposed to. By "magnetization" herein is meant the magnetic moment per volume, typically measured in Bohr magnetons per unit volume. By magnetic field gradient hereby is meant a variation in the magnetic field with respect to a position. By magnetic force density herein is meant the magnetic force a particular particle encounters at its specific position. Gradi-

ents of about 10 T/m to 1000 T/m are generally appropriate for the separation of materials discussed herein, although in some cases a stronger or weaker gradient may be used.

[0062] In order to capture the magnetic or magnetically labeled materials, the time that takes the material to reach the surface of the channel or the matrix also has to be greater than the residence time of the material in the channel. The longer the distance from the initial location of the material to the channel wall or the surface of the matrix, the longer it takes the material to reach the wall. The residence time of the material in the magnetic microchannel depends on the flow rate of the sample. A slow flow rate will allow the magnetic or magnetically labeled material to stay longer in the magnetic microchannel, thus providing the material with more time and opportunity to be captured. The flow rate can be adjusted to balance capture efficiency with shear rate. A higher shear rate will generally result in cleaner separations but lower capture efficiency. The flow of the fluid may also be stopped temporarily if necessary.

[0063] In a preferred embodiment, the magnetic microchannel comprises magnetic beads. By "magnetic beads" herein is meant magnetically susceptible beads that are capable of producing high magnetic filed gradients in the channel when magnetized by an external magnetic field.

[0064] Materials for the magnetic beads include, but are not limited to, ferromagnetic, ferrimagnetic, or paramagnetic materials.

[0065] Ferromagnetism occurs when unpaired electrons in the material are contained in a crystalline lattice thus permitting coupling of the unpaired electrons. Ferromagnetic materials are strongly susceptible to magnetic fields and are capable of retaining magnetic properties when the field is removed. Preferred ferromagnetic materials include, but are not limited to, iron, cobalt, nickle, alloys thereof, and combinations thereof. Other ferromagnetic rare earth metals or alloys thereof are also suitable. The most preferred embodiment is nickel and alloys thereof because of its high chemical resistence and high magnetic permeability for very pure iron. In one embodiment, saw-tooth structures, described further below, were used and coated with a nickel-iron permalloy having a very high magnetic permeability.

[0066] In a preferred embodiment, the magnetic beads are very fine, typically about 10 to 500 μm. The relationship between the particle size and the magnetic force density produced by the particles in response to an external magnetic field is given by the equation

$$f_m = B_0 I \; \mathrm{grad} \; H \; I = B_0 M/a$$

[0067] where f_m is magnetic force density, B_0 is the external magnetic field, $I \; \mathrm{grad} \; H \; I$ is the expression for the local gradient at the surface of a magnetic bead, M is the magnetization of the matrix element, and a is the diameter of the bead. Accordingly, the finer the magnetic beads, the higher the magnetic gradient and thus the higher a magnetic force density will be produced at the surface of the magnetic microchannel. Smaller beads will produce stronger gradients, but their effects will be more local. Generally, in a deeper channel only larger beads will produce gradients across the channel. This will allow the capture of very fine and weakly magnetized materials and increase the efficiency of magnetic capturing.